WILSON

The Ammonia, Phosphate, Chloride and Acid Concentration of the Urine of a Fasting Man

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THE AMMONIA, PHOSPHATE, CHLORIDE AND ACID CONCENTRATION OF THE URINE OF A FASTING MAN

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I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY

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THE AMMONIA, PHOSPHATE, CHLORIDE AND ACID CONCENTRATION OF THE URINE OF A FASTING MAN.

D. Wright Wilson.

HISTORICAL

Numerous investigations have been made on fasting men and a large amount of valuable data has been collected though few attempts have been made to correlate the excretion of the substances we wish to consider.

Benedict (1), in his masterly fasting studies, determined the excretion of phosphates and chlorides. The phosphate output increased to a maximum on the first to fourth day of the fast in various experiments. In general, the chloride excretion was considerable for the first two days with a marked decrease on the third day. Thereafter, the elimination tended to diminish but with considerable variation. He also observed that where the volume of ingested water was over 1000cc., the volume of urine was not far from that of the water consumed.

Cathcart (2), in his work on Bauté, showed an increased excretion of ammonia during the fast which reached a maximum on the eighth day and decreased thereafter. The acidity and phosphate output ran parallel, reaching a maximum on the third day and diminishing gradually during the remainder of the fast. The chloride excretion decreased steadily . The amount excreted of all four constituents dropped suddenly to a minimum value during the starch and cream diet and increased toward

the normal upon the return to the original high protein diet. There was a retention of 10 to 11 grams of chlorides.

Van Hoogenhuyze and Verploegh (3) determined the acidity, phosphate and chloride output in an experiment on Tosca. The acidity reached a maximum on the third day of the fast while the phosphate excretion was highest on the fourth. Thereafter there was a general, though irregular, decrease in the output of both constituents. As in Cathcart's experiment, their excretion diminished immediately when food was given. The chloride output decreased suddenly on the first day of the fast and showed marked fluctuations thraughout, with the minimum values near the middle of the fast.

Experiments on Succi, in which he fasted thirty days for Luciani (4) and twenty-one days for Ajello and Solaro (5), show the acidity and phosphate output running parallel with a maximum on the fifth day followed by a gradual decrease. The chloride excretion gradually diminished with considerable oscillation. There was a marked retention of phosphates and chlorides during the first feeding days after the latter fast. During the last ten days of the former fast sugar, gelatine and peptone were fed.

E. and O. Freund (6) report another twenty-one day fast by Succi in which the acidity increased on the second day and decreased thereafter while the phosphate excretion was highest on the first day and diminished throughout the fast. The ammonia output decreased during the first three days, ,then rose to a maximum and diminished to a low value during the

remainder of the experiment.

Lehmann, Müller, Munk, Senator and Zuntz (7) publish results of experiments on Cetti, fasting ten days, and Breithaupt, fasting six days. In both cases, the acidity and phosphate output rose to a maximum on the third day and decreased steadily thereafter. The chloride excretion in the former case rose to a maximum on the second day and decreased during the remainder of the fast, while in the latter experiment it diminished steadily throughout.

Brugsch (8) determined the various constituents in the last seven days of a thirty day fast of Succi. He found a high ammonia output (35% of total nitrogen), the chloride and phosphate excretion low but fairly constant and the acidity diminishing.

Hoover and Sollman (9) report a case of fasting during hypnotic sleep in which the phosphate excretion increased to a maximum on the final day and the chloride output decreased to about half its original value during the fast.

DESCRIPTION

Purpose. The purpose of this experiment was to determine, if possible, any relations between the ammonia, phosphate, chloride and acid concentrations of the urine during a fast and during subsequent low and high protein feeding periods.

Subject. The subject (E) was a man weighing 76.6 kilograms at the beginning of the fast. He was an instructor in

the Chemistry Department of this University and had previously(10) been a subject in a fasting experiment of similar length carried out in this laboratory. During the fast, he kept up his daily routine of work as instructor.

Diet. The diet, described in a previous paper (11), for the preliminary and final periods, consisted of 600 grams graham crackers, 1350 grams whole milk, 75 grams butter, 150 grams peanut butter, 1050 cc. water (300 cc. at meal time and 750 cc. between meals). This diet contained 21.86 grams of nitrogen (136 grams protein) with an energy value of about 6000 Calories which gave the subject 1.77 grams protein and 80 Calories per kilogram of body weight. The fast was seven days in length with a daily water ingestion of 1500 cc. Following the fast, was a low-protein period of four days during which 5.23grams nitrogen or about one-fourth of the regular diet was ingested daily. The subject also received 1500 cc. water daily. The diet for the final period was the same as that for the preliminary period.

The Collection of Urine. The urine was collected in 24 hour periods and kept in a refrigerator in two-liter acid bottles. Thymol was used as a preservative.

Methods of Analysis. The methods of analysis were as follows: ammonia, Folin; total acidity, Folin; phosphates, Uranium Acetate titration; chlorides, Clark's modification of Dehn's method.

GENERAL DATA

Subject E

Day of Exp	Vol. urine cc	Total N grams	Ammonia N grams	Acidity cc.N/10 NaOH	P_2O_5 grams	Chloride grams NaCl	NH_3 % Tot.N	$\frac{P_2O_5}{Acidity}$
				Preliminary Period				
1	1200	17.532	0.185	24.52	2.683	7.996	1.05	0.109
2	1350	17.706	0.177	24.52	3.358	10.232	1.00	0.137
3	1210	17.649	0.158	24.67	2.503	9.801	0.89	0.101
4	1150	17.772	0.209	21.72	2.527	8.000	1.18	0.116
Av.	1228	17.665	0.182	23.86	2.768	9.007	1.03	0.116
				Fasting Period				
1	990	14.395	0.344	32.89	2.616	5.035	2.39	0.079
2	1345	17.743	0.747	67.71	2.509	3.231	4.21	0.037
3	1540	19.534	1.113	77.04	2.851	2.539	5.70	0.037
4	1340	16.096	1.388	66.42	2.490	1.253	8.62	0.037
5	1410	13.284	1.390	52.50	2.376	1.474	10.46	0.045
6	1015	13.038	1.463	46.24	1.186	1.132	11.22	0.026
7	1120	12.695	1.394	43.89	0.955	1.137	10.98	0.022
Av.	1251	15.255	1.120	55.24	2.140	2.257	7.65	0.040
				Low Protein Final Period				
1	900	11.213	1.479	21.48	0.951	0.874	13.19	0.044
2	1000	8.621	0.552	14.06	0.537	0.714	6.40	0.038
3	1240	8.149	0.370	14.34	0.822	0.710	4.54	0.057
4	1330	8.642	0.217	13.62	1.246	0.762	2.51	0.091
Av.	1118	9.156	0.655	15.88	0.889	0.765	6.66	0.058
				High Protein Final Period				
1	970	14.131	0.161	21.20	1.830	1.404	1.14	0.086
2	1420	15.153	0.158	20.55	2.934	6.322	1.04	0.142
3	2530	13.960	0.241	22.80	2.778	14.063	1.73	0.122
4	1550	13.909	0.207	19.96	2.332	10.220	1.49	0.117
5	2175	15.860	0.204	22.87	2.587	13.029	1.29	0.113
Av.	1729	14.602	0.194	21.48	2.492	9.008	1.34	0.116

EXPERIMENTAL

Preliminary Feeding Period. The subject was placed on a uniform diet which contained 21.86 grams nitrogen per day. The preliminary feeding period lasted four days during which a satisfactory nitrogen equilibrium was maintained. The urine volume and the various constituents under consideration were excreted in fairly constant amounts and furnish a normal average for comparison.

Fasting Period. During the fast, the subject continued his regular activities as instructor. 1500 cc. water were taken daily. The urine volume was low on the first day, rose on the second and remained fairly constant with a slight decrease toward the end of the fast. The average was nearly the same as that of the preliminary period.

The ammonia excretion increased on the first day of the fast and rose rapidly at first, and then slower, to a maximum on the sixth day of 1.463 grams nitrogen, nearly ten times the average of the preliminary period. The relative increase was slightly greater. On the last day of the fast the value dropped to 1.394 grams.

The acid output rose immediately on the first day of the fast, more than doubled itself on the second day and was still higher on the third. Thereafter, there was a gradual decrease to the end of the fast.

The phosphate excretion increased slightly on the first day, dropped on the second but reached a maximum on the third.

After the third day, the values decreased steadily.

The chloride excretion was less than normal at the outset of the fast and decreased rapidly for three days, after which time there was a slower and less steady diminution.

Low Protein Feeding Period. At the close of the fasting period, the subject was placed on a diet similar to that of the preliminary period but only one-fourth that amount so that, for four days after the fast, the subject received 5.23 grams nitrogen and about 1800 Calories daily. The urine volume was low on the first day but increased gradually giving an average for the period of a little below normal.

The ammonia nitrogen was higher on the first day of the low protein feeding period than the last day of the fast and was, indeed, slightly higher than the maximum value for the fast. A marked decrease was observed on the second day, the value dropping from 1.479 grams to 0.552 grams with a continued decrease each day following. The minimum value, however, was somewhat higher than any value in the preliminary period.

The acidity dropped immediately after the fast to a value lower than any observed in the preliminary period and decreased further with a minimum value for the experiment on the fourth day. The excretion of phosphates diminished slightly on the first day with a considerable decrease on the second, after which there was a steady and rapid increase to a value about half that of the preliminary period. The chloride excretion dropped considerably on the first day and decreased somewhat on the next and stayed about this minimum value for the re-

mainder of the period.

Final Period. The final period consisted of five days during which the food intake was increased to the amount eaten in the preliminary period. The urine volume was again low on the first day but rose rapidly to a maximum value on the third day and then decreased to a value above the normal. The average was considerably above that of the preliminary period.

The ammonia output continued to decrease for the first two days but showed a marked rise on the third from 0.158 grams to 0.241 grams, an increase of over 52 per cent. On the fourth and fifth days, the values were decreased to somewhat above the average of the preliminary period.

The acid output increased on the first day of the final period to a value somewhat below the normal and showed no great variation throughout the period.

The phosphate excretion increased rapidly, giving values on the second and third days above the normal. For the remainder of the period, the output was somewhat below the average of the preliminary period.

The output of chlorides rose rapidly for the first three days of the final period and reached a maximum of 14 grams on the third day. The values for the last three days showed considerable variation and were all higher than the average of the preliminary period.

GENERAL DISCUSSION

Data have been presented of a fast of a man for a period of seven days with subsequent low and high protein feeding periods.

The urine volumes varied within normal limits throughout the experiment. There was, however, a considerable diminution on the first day of each period. The volumes were below a liter on these days only. In each case, there was a marked retention for the daily water intake was 2225 cc. for the preliminary and final periods, 1500 cc. for the fast and 1892 cc. for the low-protein period.

On the third day of the fast, the urine volume was 1540 cc. which was 40 cc. more than the water intake. This was the only time during the fast when the volume of liquid excreted was larger than the volume ingested. Our data, in this respect, are comparable with Benedict's (1) observation that when the volume of ingested liquid exceeds 1000 cc., the urine volume is not far from that of the liquid ingested. The average urine volume was higher for the fast than for the preliminary period.

In the low protein period, there was a steady increase from the minimum on the first day. The volumes in the final period increased daily from the minimum on the first day to the maximum for the experiment on the third day when the volume of urine was again greater than that of the ingested liquids.

The ammonia output rose immediately on the first day of the fast and increased rapidly, both absolutely and relatively, to a

maximum value on the sixth day, which was eight times the average for the preliminary period. There was a slight decrease on the seventh day.

This increased elimination of ammonia during the fast has been frequently observed by various investigators and explained as due to acidosis caused by the formation of the acid products of fat metabolism. In fasting, the body must draw on its own stores of glycogen and fat for energy and, as the fat is metabolized, the acid products formed, diacetic and b-oxybutyric acids, accumulate so rapidly that a condition of acidosis is established which calls for an increased formation of ammonia to aid in maintaining the normal reaction of the body fluids. In this consideration, it is interesting to compare the figures we have obtained for ammonia, acidity and phosphates as excreted in the urine during and following the fast.

The values of all three constituents were increased at the beginning of the fast. The ammonia output rose rapidly to a maximum on the sixth day; the acidity increased to a maximum on the third day and then gradually decreased; the phosphate output increased in general to the third day and then decreased, the relative decrease being closely parallel to the acidity. Cathcart (2), Van Hoogenhuyze and Verploegh (3), Benedict (1), Luciani (4), Ajello and Solaro (5), Munk (7) and others report similar results in the constituents which they determined.

The explanation of these relations may lie in the complicated mechanism by which the body attempts to maintain a

uniform reaction of the body fluids. As soon as the fasting starts, the glycogen and fat stores of the body are called upon to furnish the necessary energy for the body. At first, the glycogen is used in large amounts, the fats being called upon more and more as the fast progresses. Thus, on the first day, the acids formed by fat metabolism were produced in small amounts only, which called for but a slight increase in the ammonia formation and a slightly increased acid and phosphate output.

Henderson's work (12) on the relation of phosphates to the maintenance of neutrality of the body fluids shows that they play an extremely important role. As acids are formed in the body and pass into the blood or lymph, an equilibrium is immediately established, some of the disodium phosphate present changing to monosodium phosphate. An excess of monosodium phosphate in the blood is excreted by the kidneys, due either to an increased tendency to dialyze as shown by Maly (13), or to a function of the kidneys or both. Thus, an increased phosphate excretion with increased urine acidity follows an increased formation of acids in the body. Just such a condition was met with in our experiment. The acids formed by fat metabolism caused increased excretion of phosphates with increased urine acidity.

After the glycogen stores were depleted, the fat metabolism became more marked as shown by a greater increase in the ammonia output on the second day when the excretion was more

than doubled. The ammonia formation did not, however, keep pace with the acid formation as indicated by the increased acidity of the urine on the second day of the fast. The low value of the phosphate output is unexplained. The third day showed an increased excretion of all three constituents. Thereafter, the ammonia increased but the acidity and phosphate output decreased, indicating that the production of ammonia had caught up with the acid production within the body and was gradually exceeding it. With the increase of ammonia, there would be a smaller amount of free acids to be eliminated and therefore a decreased urine acidity. The ammonia excretion reached a maximum on the sixth day and decreased on the seventh which may have been caused by decreased fat metabolism due to a lessening of the fat stores of the body.

Throughout the fast and the low-protein feeding period, the ratio of phosphates to acidity of the urine is much below the normal, showing a retention of phosphates and a higher excretion of free acids than usual. This explanation is confirmed by the extremely low ratio on the final days of the fast when there was a considerable excretion of diacetic and b-oxybutyric acids and, without doubt, a marked deficiency of phosphates in the body.

On the first day of the low-protein feeding period, the ammonia output increased considerably, exceeding slightly the maximum value of the fast. This may have been due to an attempt of the organism to reduce the acidosis of the body. As a

result of this high ammonia excretion and of the food given, the acidity dropped to less than half the value of the previous day. The phosphate output remained nearly stationary, causing an increase in the ratio of phosphates to acidity which was probably due in part to the immediate decrease in the formation of acids in the body.

The diet seemed sufficient to overcome much of the acidosis, as the ammonia output decreased nearly one-third on the second day and diminished thereafter to the end of the period. The acidity of the urine decreased in general with a slight increase on the third day. The phosphate output diminished nearly one-half on the second day, the increased slowly to the end of the period. This retention has been noted by Cathcart, Benedict, and Van Hoogenhuyze and Verploegh and may indicate a tendency on the part of the body to regain its normal amount of phosphates. The ratio of phosphates to acidity increased toward the normal.

With the high-protein ingestion, there was an immediate decrease in the ammonia excretion. The outputs of the first two days were rather below the normal average but on the third day, the excretion increased more than fifty per cent, with a return to slightly above normal for the remainder of the period. The high value on the third day has been noted before in experiments (10) in this laboratory and in certain other data, especially in Cathcart's work on Baute. In the latter experiment, a slight rise occurred on the third day of normal feeding following two days of non-nitrogenous food ingestion. This rise

has been explained as due to an attempt on the part of the body to free itself of the last traces of acidosis so that it may return to a normal metabolic regime. This explanation gains support from the fact that on this day there was also a high excretion of acids and phosphates.

By examining the data for the low-protein period, we note that no increase occurred but instead, a continuous decrease. The non-appearance of the rise of the ammonia excretion on the third day of this period may have been due to the fact that the food ingested, being but one-fourth the amount of the normal diet, was low not only in nitrogen but also in calorific value and the body was still forced to derive a part of its energy from its own fat supply, thus allowing a continued, though decreased formation of acids from fat metabolism and a continued state of acidosis.

The chloride output throughout the experiment seemed to bear no relation to the excretion of the other constituents considered. It decreased rapidly during the first four days of the fast and remained fairly constant for the remainder of the period with a slight diminution. In the low-protein feeding period, the excretion dropped to less than one-tenth of the normal output, showing a considerable retention. A similar retention has been observed in a number of experiments as previously noted.

SUMMARY

Data are given for the ammonia, phosphate, chloride and acid excretion of a man during a seven day fast and during subsequent low- and high-protein feeding periods.

There was a marked retention of water on the first day of each period. The daily urine volumes were somewhat lower than the daily intake of water except on the third day of the fast and the third day of the final period when the excretion was slightly in excess.

A condition of acidosis was indicated by the increased output of ammonia which rose to a maximum on the sixth day of the fast. There was a marked diminution in the ammonia excretion when food was given.

The acidity and phosphate output rose to maxima on the third day of the fast and then decreased. After the fast, the acidity decreased and the phosphates showed considerable retention.

The relations between the ammonia, acid and phosphate excretion in the urine show the complicated but definite way in which each aids in preserving the normal reaction of the body fluids.

After the high excretion of ammonia on the third day of the final period, there was a return to slightly above normal. Both phenomena were absent in the period of low-protein ingestion where the amount of food eaten was one-fourth that of the normal diet.

The chloride excretion decreased rapidly during the first

four days of the fast and remained nearly constant with a slight decrease. During the low-protein feeding period and the first day of the high-protein period, there was a marked retention.

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